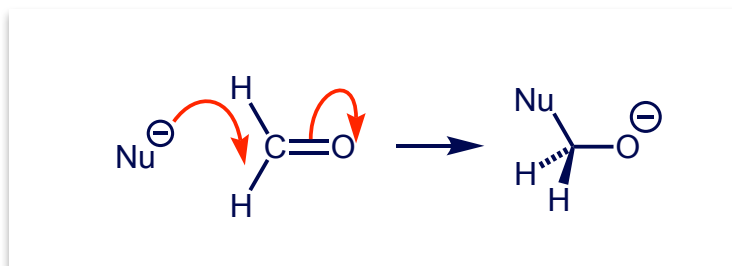


Introduction to Organic Chemistry

Handout 3 - Mechanism



<http://burton.chem.ox.ac.uk/teaching.html>

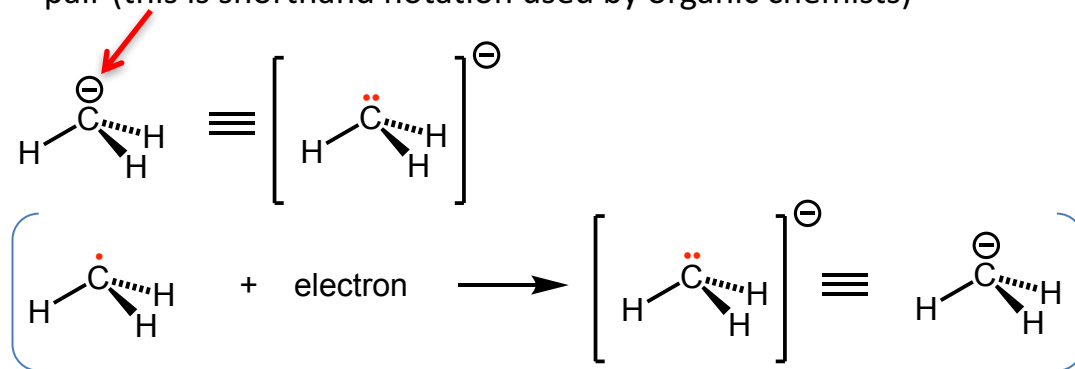
- *Organic Chemistry* J. Clayden, N. Greeves, S. Warren
- *Stereochemistry at a Glance* J. Eames & J. M. Peach
- *The majority of organic chemistry text books have good chapters on the topics covered by these lectures*
- *Elie* Stereochemistry of Organic Compounds (advanced reference text)

■ **acid base reactions**

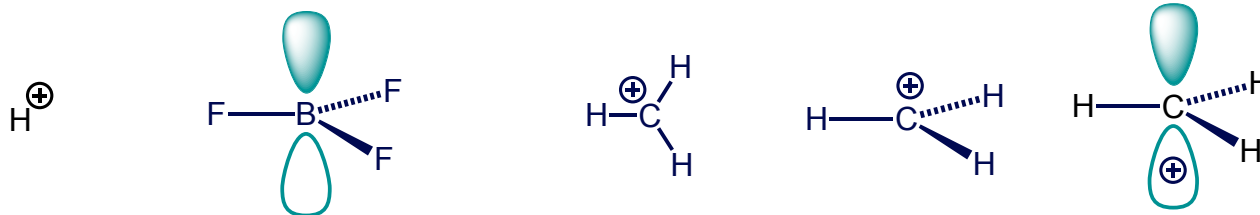
■ a Lewis base is an electron pair donor
(can be charged or neutral)



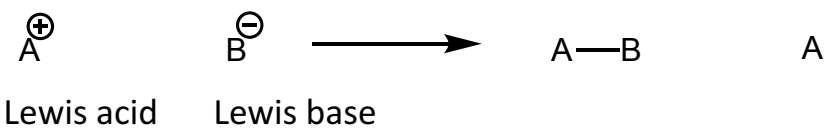
when atom is negatively charged, the negative charge implies a lone pair (this is shorthand notation used by organic chemists)



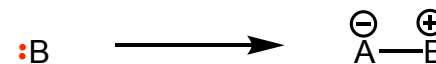
■ a Lewis acid is an electron pair acceptor (can be charged or neutral)



■ acid base reactions



B is sharing an electron pair and therefore becomes positively charged

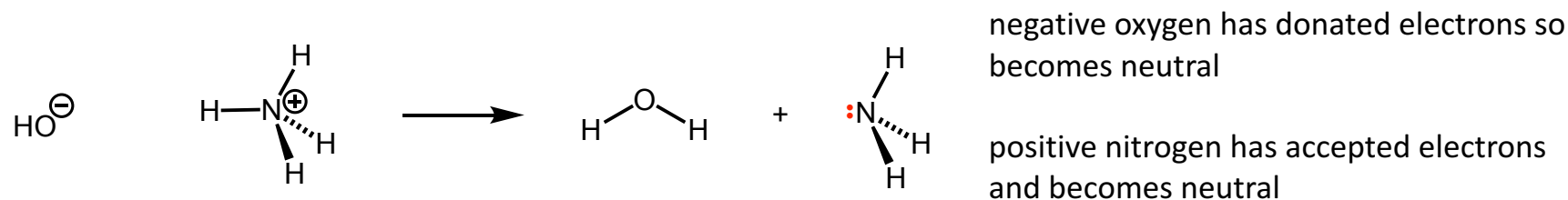
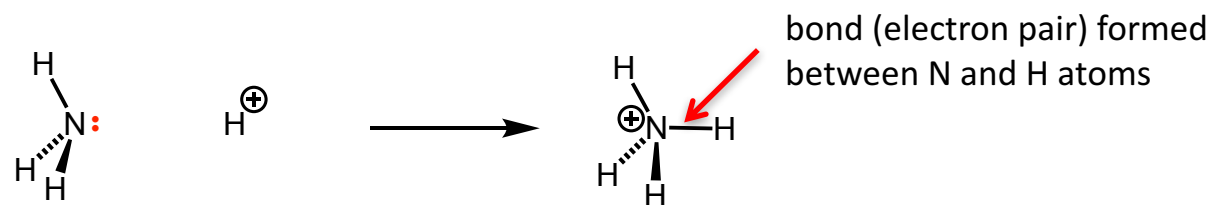


A is accepting an electron pair and therefore becomes negatively charged

■ conservation of charge

CURLY ARROWS – indicate the movement of a *pair* of electrons

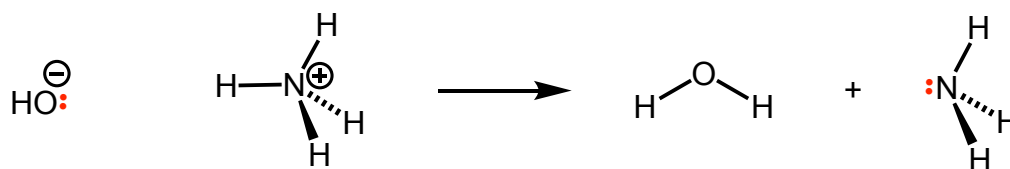
■ the arrow starts at the origin of the pair of electrons (lone pair or bonding pair) and the head of the arrow indicates where the electrons end up (lone pair or bonding pair)



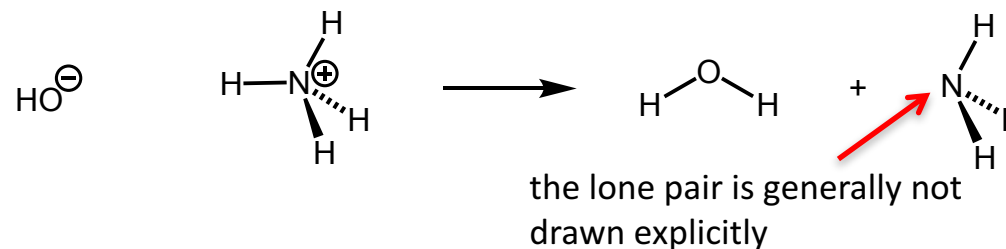
1st curly arrow starts from the negative charge which we treat as a lone pair

2nd curly arrow starts from the N–H bond pair

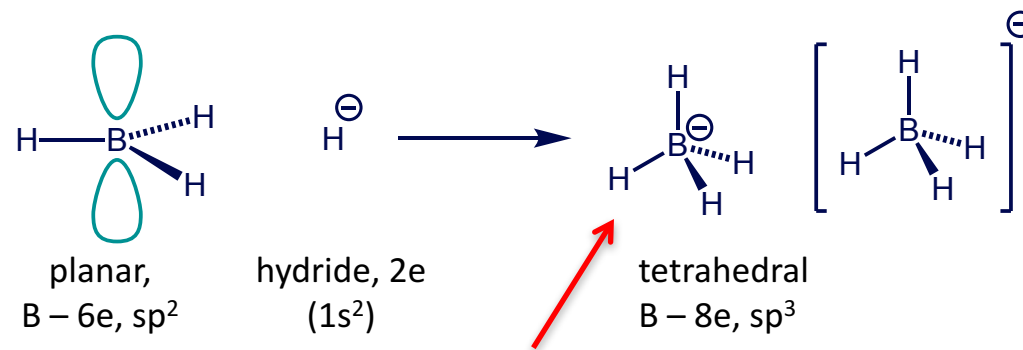
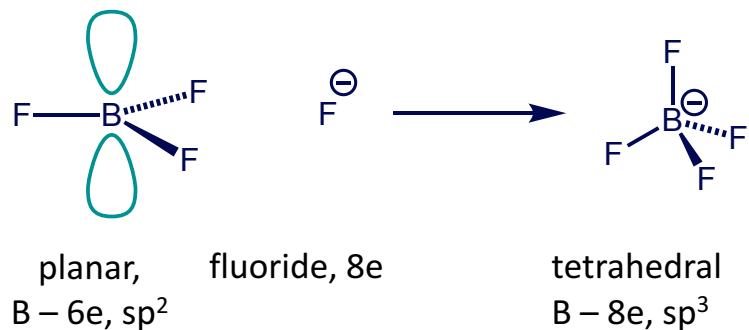
■ strictly speaking the arrow starts from an actual lone pair but it is normal practice to draw it from the negative charge



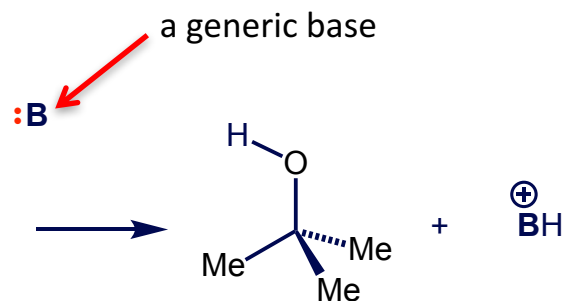
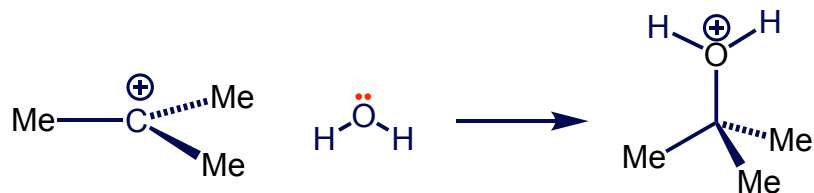
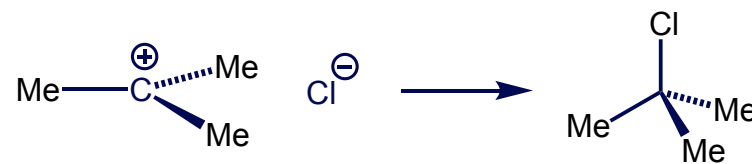
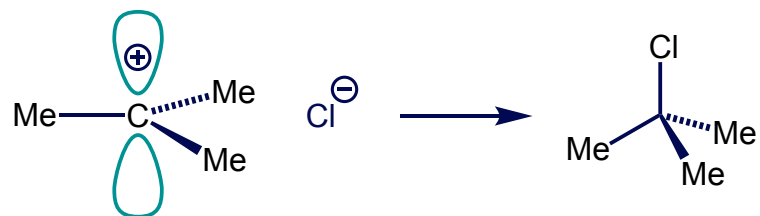
■ drawing the curly arrow to point at the atom to which it is forming a bond is also common practice



acid base reactions



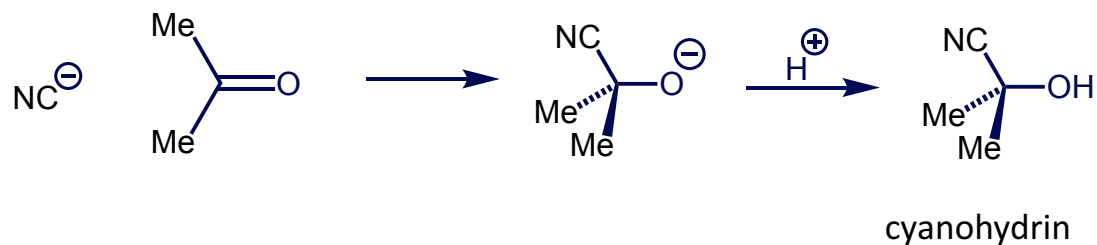
here the negative (formal) charge (although drawn on boron) does not represent a lone pair – B has 8 electrons from the bonding pairs



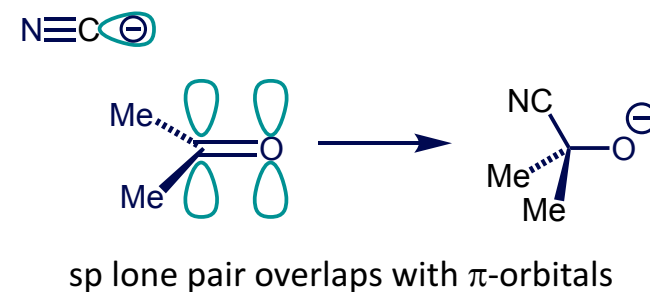
■ a common error

~~X~~
 H^+
 a curly arrow cannot begin from a proton – H^+ has no electrons

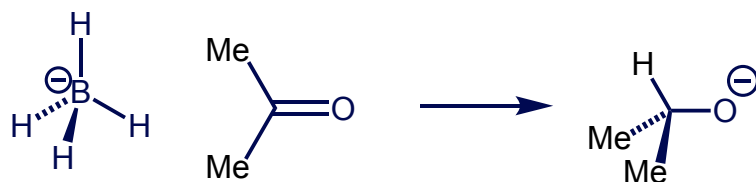
■ further examples – some typical reactions of aldehydes and ketones



■ orbitals

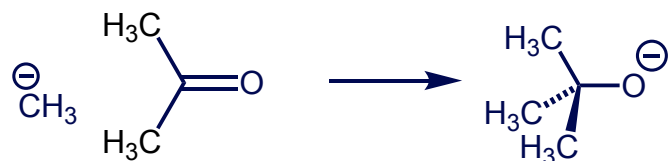


■ $\text{Li}^+ \text{AlH}_4^-$ or $\text{Na}^+ \text{BH}_4^-$

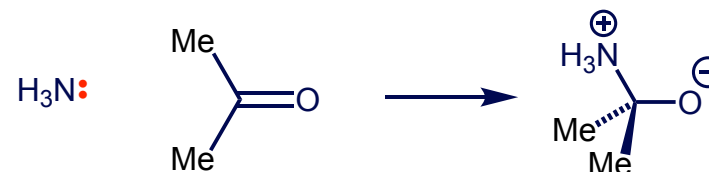


■ arrow comes from a bond pair of electrons and transfers hydrogen with its pair of electrons i.e. as hydride H^-
(remember the negative charge on B does not represent a lone pair)

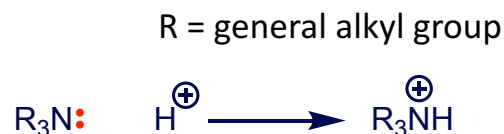
■ addition of a Grignard reagent – $\text{CH}_3\text{-MgBr}$



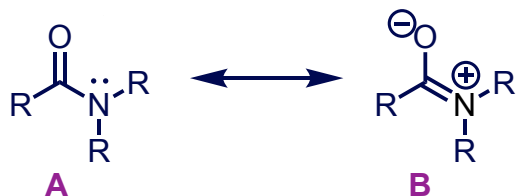
■ addition of a neutral nucleophile



- delocalisation a.k.a resonance



- amines are basic – the nitrogen lone pair is readily protonated
- amides, however, are essentially neutral – the lone pair is delocalised into the carbonyl group



- lone pair in **A** is bonding pair in **B**

- neither **A** nor **B** actually exist – the real structure is a weighted average of structures **A** and **B** called a resonance hybrid

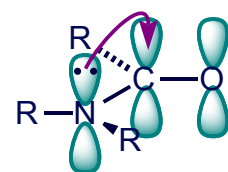
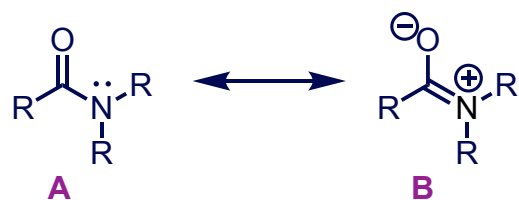
- structures **A** and **B**, are referred to as *resonance* structures

- note* – there **is not** an equilibrium between **A** and **B**

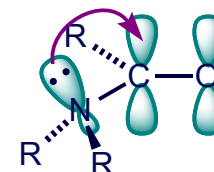
- individual Lewis structures do not accommodate the electron distribution in certain functional groups, and delocalisation (a.k.a. resonance) is a simple method to account for the actual electron distribution

- effect on structure

- the curly arrows above represent the overlap of the nitrogen lone pair with the C-O π -orbitals
- the best overlap occurs if the N-lone pair is in a p-orbital, i.e. N is sp^2 hybridised

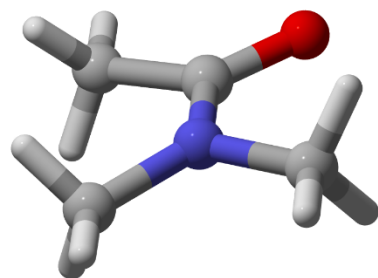


N- sp^2 hybridised
N-lone pair in p-orbital

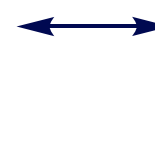
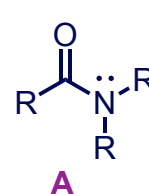
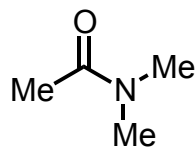


N- sp^3 hybridised
N-lone pair in sp^3 -orbital

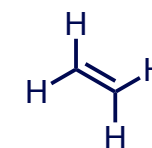
- the curly arrows above represent the overlap of the nitrogen lone pair with the C-O π -orbitals (the antibonding π^* orbital)
- the best overlap therefore is if the N-atom is sp^2 hybridised resulting in the N-lone pair being in a p-orbital with excellent overlap with the p-orbitals of the C–O π -system
- if the N-atom were sp^3 hybridised then the N-lone pair would be in an sp^3 orbital which would result in poorer overlap with the adjacent C–O π -system
- generally better overlap (of full and empty orbitals) = greater stabilisation
- actual structure is composite of **A** and **B** – the geometry of amides is planar



X-ray crystal structure of dimethyl acetamide



restricted rotation
around C–N bond



C–N bond length: amines 1.47 Å, amides 1.33 Å

- some guidelines for drawing delocalised structures (resonance structures, canonical forms)

- all resonance structure must be proper Lewis structures

- the positions of the nuclei must be the same in all structures

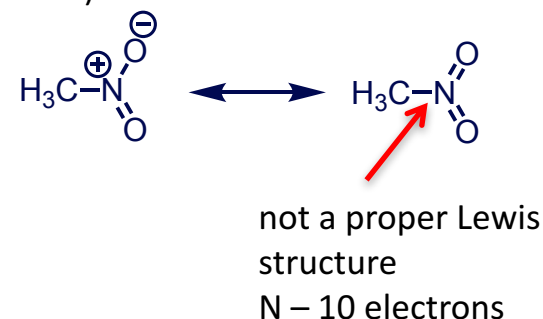
- all structures must have the same number of paired/unpaired electrons

- all atoms involved in delocalisation should be co-planar or nearly co-planar

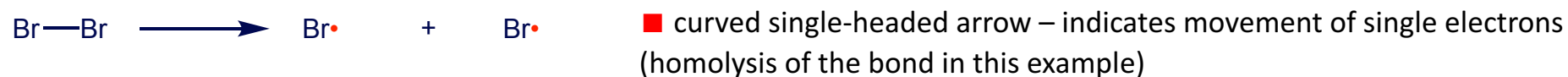
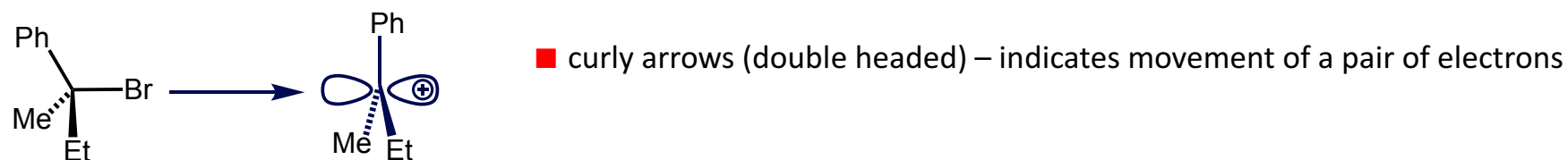
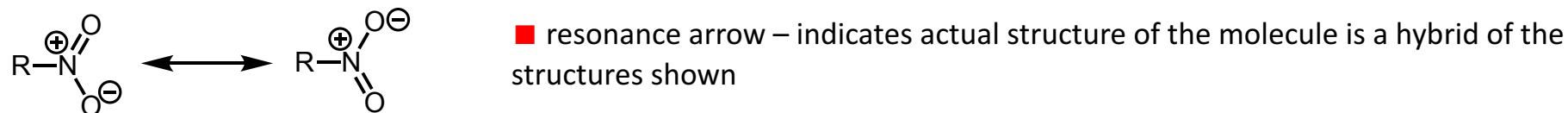
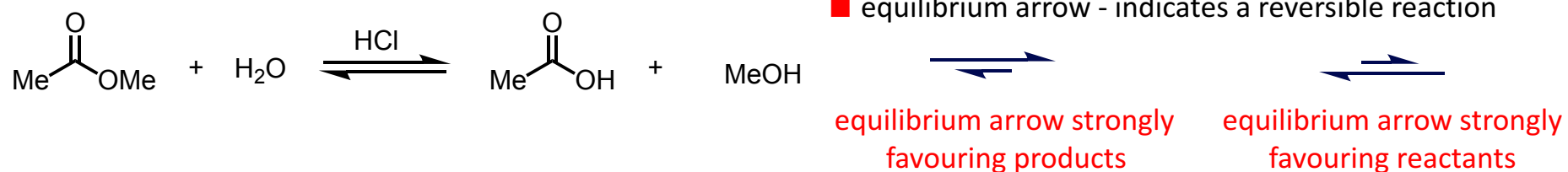
- the overall structure of the molecule is a weighted average of the various resonance structures – the more stable resonance structures contribute more to the overall structure of the molecule (and generally only the most stable resonance structures need to be considered)

- charge separation is destabilising

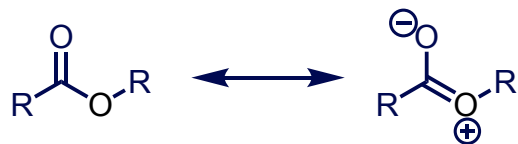
- the energy of the actual molecule is lower than any of the resonance structures



■ some of the arrows of organic chemistry

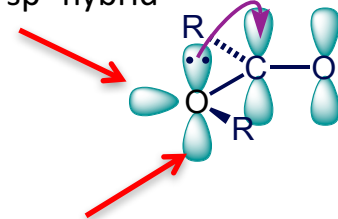


■ esters

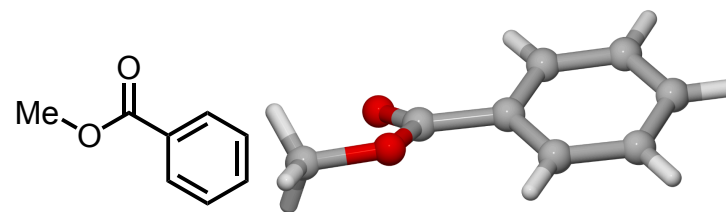


oxygen atom is sp^2 hybridised

one oxygen lone pair in sp^2 hybrid orbital

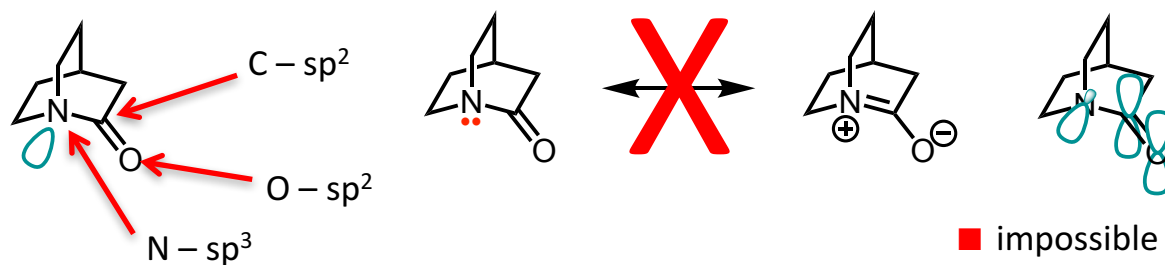


one oxygen lone pair in p-orbital

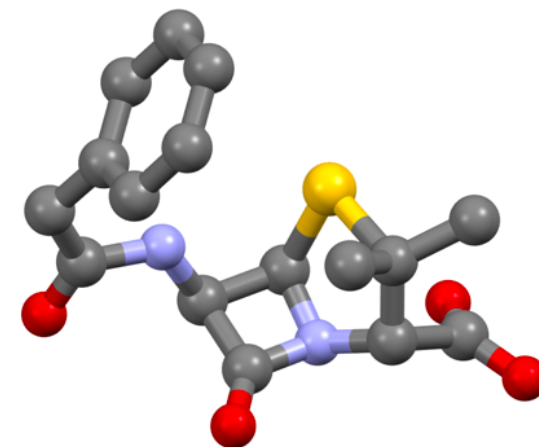


esters are generally planar

■ an unusual amide



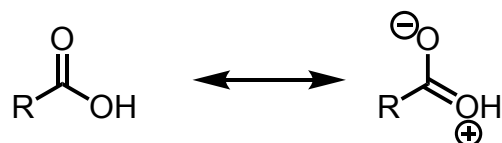
■ impossible overlap of lone pair with π -orbitals



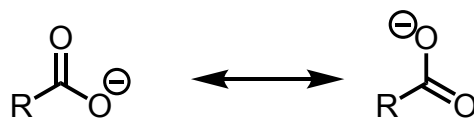
■ the above amide is much more basic than a normal amide

■ delocalisation in common functional groups

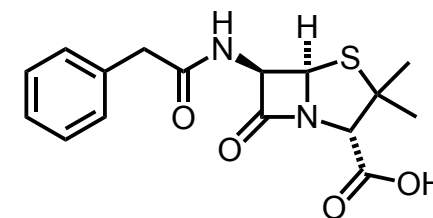
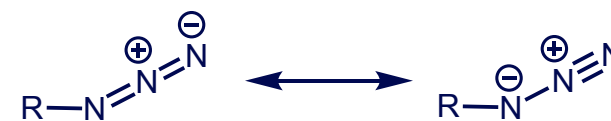
■ carboxylic acids similarly



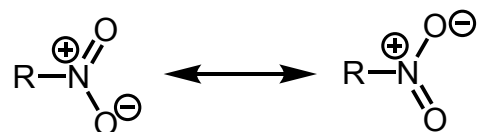
■ carboxylate



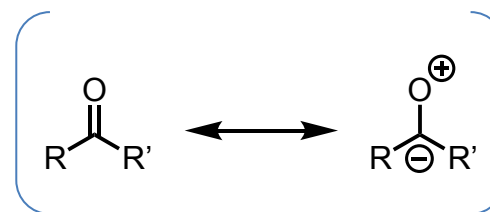
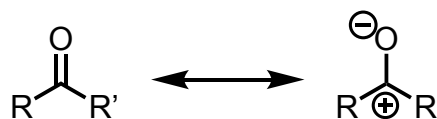
■ azides



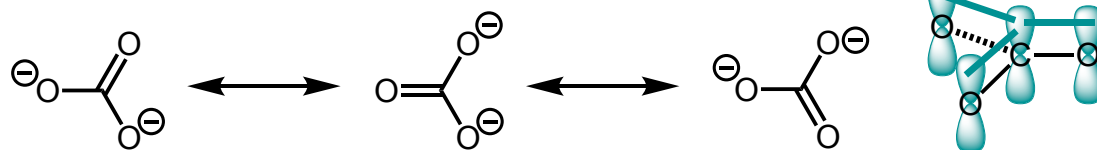
■ nitro groups



■ ketones



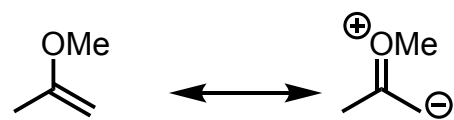
■ carbonate



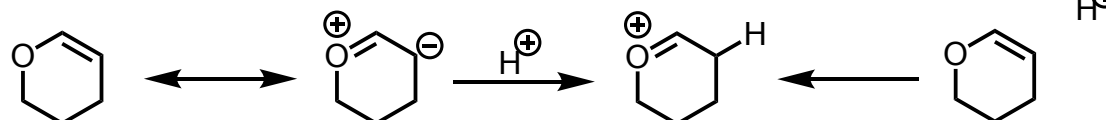
■ diazo compounds



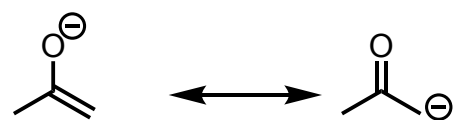
■ in general if a π -system has an adjacent atom which carries a lone pair delocalisation of the lone pair into the π -system is possible



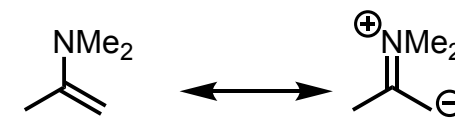
enol ether



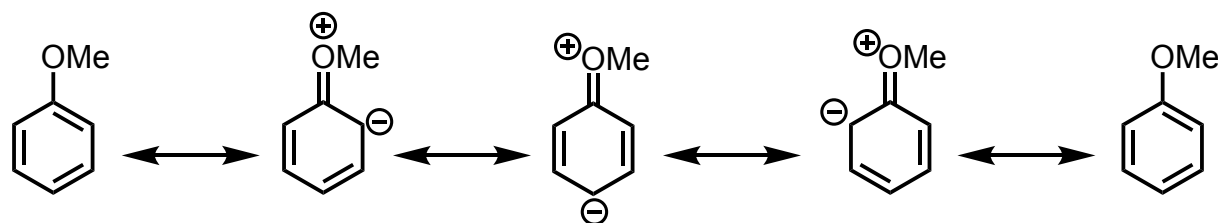
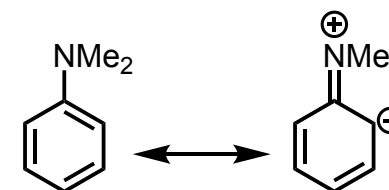
enol ether



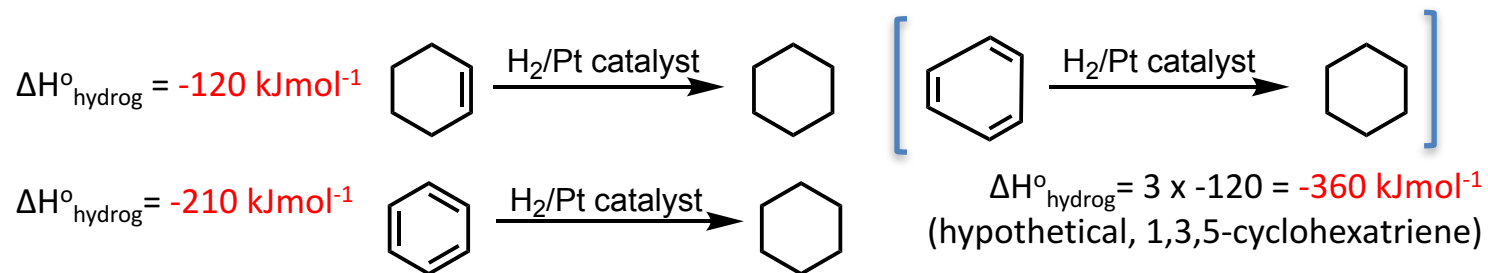
enolate anion



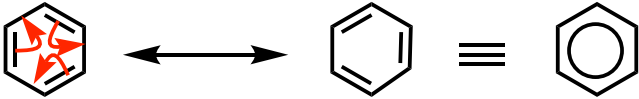
enamine



- double bond resonance
- benzene
- heats of hydrogenation



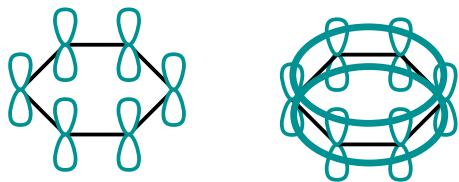
- benzene $\approx 150 \text{ kJmol}^{-1}$ more stable than expected – (represents stability over hypothetical 1,3,5-cyclohexatriene) – termed the *empirical resonance energy* (values vary enormously)



C-C	sp^3-sp^3	1.54 Å
C-C	sp^3-sp^2	1.50 Å
C-C	sp^3-sp	1.47 Å
C-C	sp^2-sp^2	1.46 Å
C-C	benzene	1.39 Å
C=C		1.34 Å
C≡C		1.21 Å

benzene best represented like this but cannot draw curly arrow mechanisms from this representation – we will therefore use the alternating double/single bond representation

- molecular orbital description



- all carbon atoms are sp^2 hybridised

- all bond angles are 120°

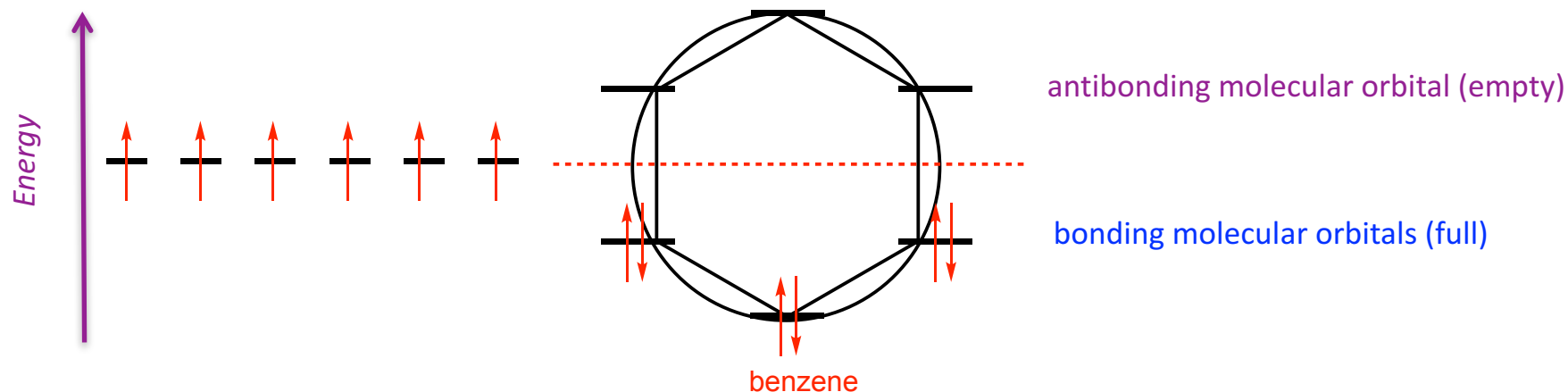
- there are six p-orbitals which overlap to give six molecular orbitals

Frost-Musulin Diagram – Frost Circle

- simple method to find the energies of the molecular orbitals for an aromatic compound

- inscribe the regular polygon, with one vertex pointing down centred at the energy of an isolated p-orbital

- each intersection of the polygon with the circumference of the circle corresponds to the energy of a molecular orbital

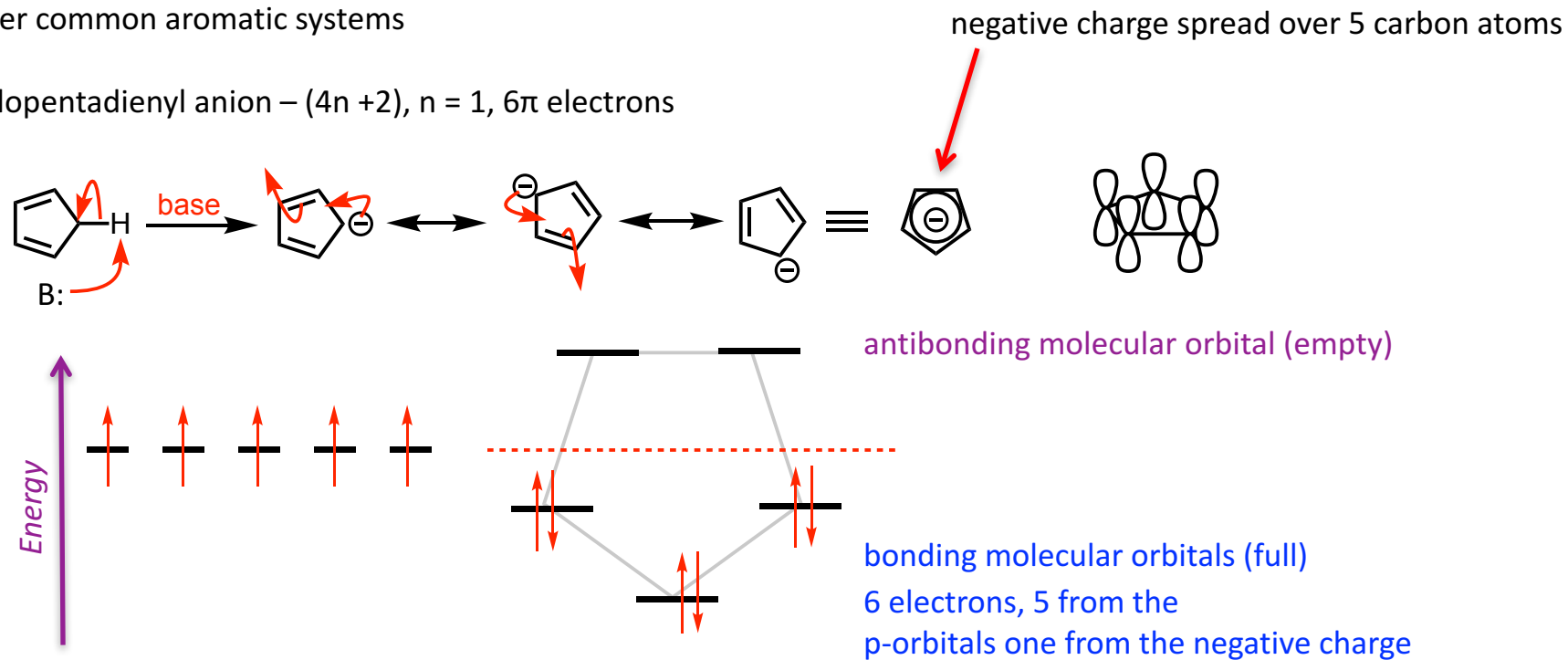


- the six electrons are delocalised over the entire ring – benzene is described as aromatic with aromatic stabilisation

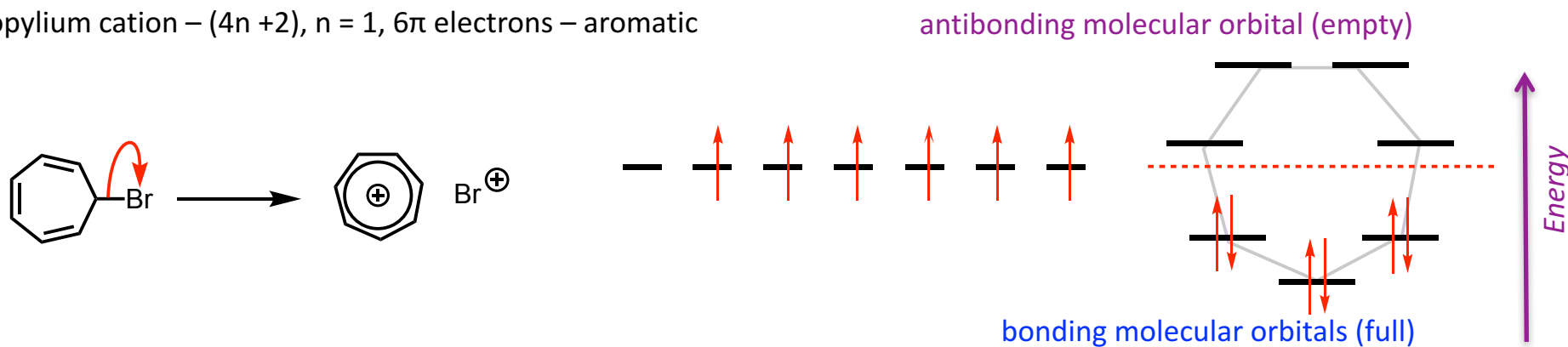
■ for aromaticity require $(4n + 2)$ π -electrons cyclically conjugated

■ other common aromatic systems

■ cyclopentadienyl anion – $(4n + 2)$, $n = 1$, 6π electrons

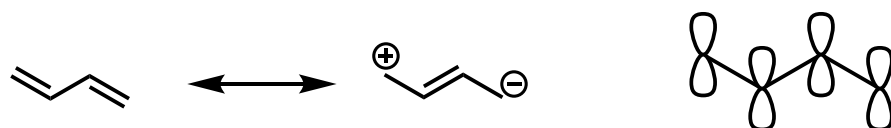


■ tropylium cation – $(4n + 2)$, $n = 1$, 6π electrons – aromatic



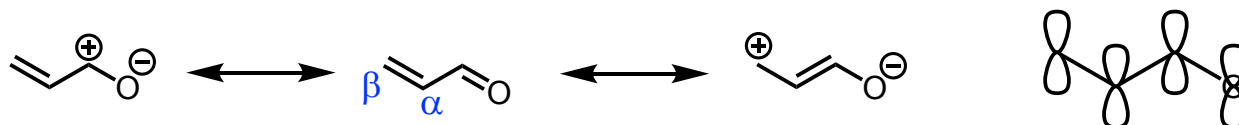
■ delocalisation in conjugated alkenes (non-aromatic)

■ dienes



■ overlap of p-orbitals on central carbon leads to new extended molecular orbital – increased bonding

■ α,β -unsaturated carbonyl compounds

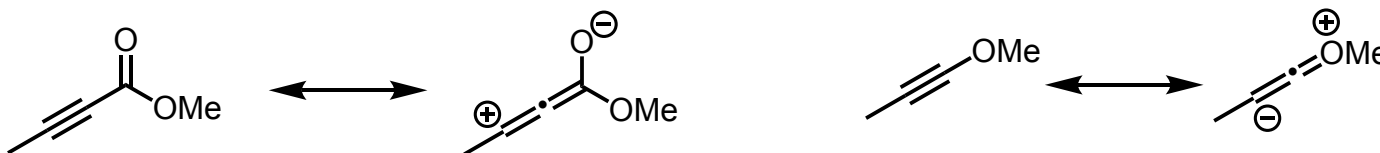


nucleophiles therefore react at the carbonyl carbon or the β -position

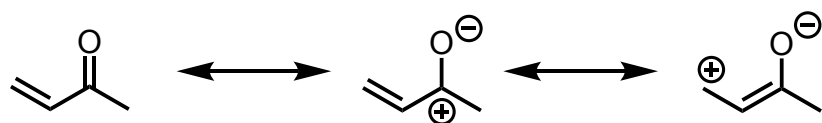
■ similar with α,β -unsaturated nitro compounds and α,β -unsaturated nitriles



■ or with triple bonded species

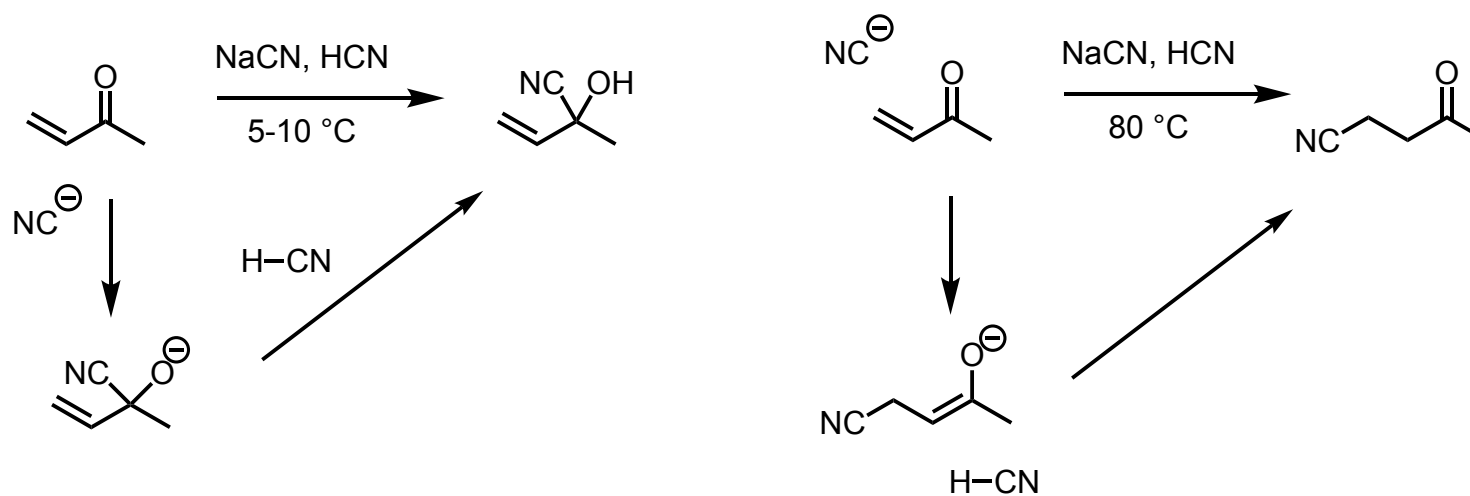


■ some more simple reactions



■ drawing delocalised structures, shows us where nucleophiles and electrophiles may attack substrates

■ cyanide will add to the carbonyl carbon, or the β -position of an α,β -unsaturated ketones depending on the reaction conditions



■ these reactions can be reversible

